Adults and Sodium: What is the relationship between sodium and blood pressure in adults aged 19 years and older?

Conclusion

A strong body of evidence has documented that in adults, as sodium intake decreases, so does blood pressure.

Grade: Strong

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here.

Evidence Summary Overview

The 2010 Dietary Guidelines Advisory Committee (DGAC) performed an updated literature search to identify new research on the relationship between sodium intake and blood pressure. The Nutrition Evidence Library (NEL) search identified 47 potential articles (15 systematic reviews/meta-analyses and 32 primary studies). A total of 13 articles, 12 primary studies and one systematic review/meta-analysis met the eligibility criteria and were reviewed. Of the 12 primary studies, nine were randomized trials (Cappuccio, 2006; China Salt Substitute Collaborative Group; Dickinson, 2009; Forrester, 2005; Gates, 2004; He FJ, 2009; Makela, 2008; Pimenta, 2009; Swift, 2005), two (He J, 2009; Schmidlin, 2007) were studies that tested different levels of sodium intake but in fixed order, and one was an observational analysis of a previously published trial (Cook, 2005). Of the 12 primary studies, eight were positive quality (Cappuccio, 2006; China Salt Substitute Collaborative Group; Forrester, 2005; He FJ, 2009; Pimenta, 2009; Swift, 2005) and four were neutral quality (Dickinson, 2009; Gates, 2004; Makela, 2008; Schmidlin, 2007). Enrollment criteria differed substantially by study, with blood pressure criteria that often bridged traditional classification schemes. Still, it appears that five of the studies enrolled normotensive individuals, six enrolled hypertensive individuals and one explicitly enrolled both normotensive and hypertensive individuals. Trials were conducted in Jamaica, Northern Chinese, US, Australia, Finland, Great Britain and Nigeria. Populations were demographically heterogeneous (e.g., enrolling black, white and Asian hypertensives living in Great Britain).

Because previous trials had already confirmed that sodium reduction lowers blood pressure, the individual trials typically addressed other issues, such as the effects of public health interventions in economically developing countries or the effects of sodium reduction on other variables (e.g., vascular function, arterial compliance, proteinuria and heart rate variability). Nonetheless, each reported the effects of sodium reduction on blood pressure. In total, a significant reduction in either systolic or diastolic blood pressure occurred in all but one of these studies, and significant reductions in both systolic and diastolic blood pressure in five studies. The eight methodologically strong studies all showed a significant reduction in systolic or diastolic blood pressure, and significant blood pressure reduction in both systolic and diastolic blood pressure occurred in five of the studies. In several studies, relatively few blood pressure measurements were obtained; hence, in some cases, the absence of significant findings might have resulted from imprecise or inadequate blood pressure measurement.

The systematic review/meta-analysis of 34 randomized controlled trials (RCTs) (He and MacGregor, 2005, positive quality), which pooled data for 23 trials of hypertensive and 11 trials of normotensive subjects, demonstrated that a modest reduction in sodium intake for four or more weeks had a significant effect on blood pressure in both hypertensive and normotensive subjects. It also found a significant dose-response relationship between sodium reduction and both systolic and diastolic blood pressure. In this meta-analysis, a median reduction in urinary sodium of approximately 1.8g per day (78mmol per day) lowered systolic/diastolic blood pressure by 2.0/1.0mmHg in non-hypertensive and by 5.1/2.7mmHg in hypertensive adults.

In aggregate, these studies reinforce and further strengthen the previous conclusions from the 2005 DGAC report that sodium reduction lowers blood pressure and benefits extend to both non-hypertensive and hypertensive individuals.

Evidence Summary Paragraphs

Cappuccio et al, 2006 (positive quality). This community-based, randomized cluster trial, conducted in 12 rural and semi-urban West African villages, examined the effect of a health promotion intervention to reduce salt intake on blood pressure (BP). Subjects included 1,013 participants (628 women, 481 rural dwellers) whose mean age was 55 years, average BP was 125/74mmHg and urinary sodium excretion (UNa) was 101mmol per day. A general health promotion intervention that covered several relevant topics was provided to all 12 villages over a six-month period. The six intervention villages received additional advice to not add salt to food when cooking, to limit specific high-salt foods and to soak other high-salt foods in water overnight before eating. Urinary sodium excretion and BP levels were assessed at three and six months for all groups. There was no significant (NS) change in urinary sodium excretion in intervention villages. At six months the intervention group experienced a non-significant reduction in systolic blood pressure (SBP) [2.54mmHg (-1.45 to 6.54)] and a significant reduction in diastolic blood pressure (DBP) [3.95mmHg (0.78 to 7.11), P=0.015), net of change in the control group. In analyses that included all participants,

regardless of intervention, there was a direct relationship between the fall in urinary sodium excretion and the fall in BP when adjusting for confounders. A difference in 24-hour UNa of 50mmol was associated with a lower SBP of 2.12mmHg (1.03 to 3.21) at three months and 1.34mmHg (0.08 to 2.60) at six months (both P<0.001). A strength of this study is the high response rate. A major limitation of the study is that it did not achieve a contrast in sodium intake. Overall, this trial should be viewed as a test of a public health intervention in a low-resource environment, not a trial to test the biologic effects of sodium reduction on BP.

China Salt Substitute Study Collaborative Group, 2007 (positive quality). This RCT, conducted in rural northern China, evaluated the long-term effects of a reduced-sodium (Na), high-potassium salt substitute [65% sodium chloride (NaCl), 25% potassium chloride (KCl), 10% magnesium sulfate] compared to normal salt (100% NaCl) on BP among 608 high-risk individuals. There were 585 subjects who completed the one-year trial, 292 in the salt-substitute group and 293 in the salt group. Mean overall difference inSBP between randomized groups was 3.7mmHg (95% CI: 1.6 to 5.9, P<0.001), and SBP was significantly lower in the salt substitute group than in the normal salt group at the six, nine and 12-month visits (all P<0.02). The magnitude of this reduction increased over time (P=0.001) with the maximum net reduction of 5.4mmHg (2.3 to 8.5) achieved at 12 months. However, there were no detectable effects on DBP at any one time point or overall. Additionally, there was no evidence of any evolution of a difference in DBP over time. Based on first-morning specimens, urinary potassium (K) was slightly higher in the salt substitute group. Strengths of the study include its large sample size, rigorous measurements of BP and high adherence, at least by self report. Limitations included lack of 24-hour urines to assess adherence, as well as impact of existing salt and salty foods that were not removed from the homes. This study is most relevant to those populations in which added sodium is the predominant source of sodium. In this case, replacement of usual table salt (100%Na) with a reduced sodium (65%), higher potassium (25%) and magnesium (10%) leads to large BP reductions in high-risk population.

Cook et al, 2005 (positive quality). This multicenter RCT, conducted in the US, examined the relationship between sodium intake and BP change in 18-month and 36-month periods using data from the Trials of Hypertension Prevention (TOHP) Phase II sodium intervention. The original TOHP II subjects were assigned to receive one of the following: Counseling for weight loss only, counseling for sodium intake reduction to 80mmol per day, counseling for weight loss and sodium intake reduction to 80mmol per day, or usual care with no study-delivered intervention. Sodium intervention and usual care groups were combined for analysis; 1,157 overweight, non-hypertensive men and women were randomized and 880 subjects completed the three-year trial (437 in the sodium reduction interventions and 443 in usual care). At 36 months, there were significant differences between the sodium reduction group and usual care group in change ofUNa excretion (-50.9mmol per day vs. -13.2mmol per day, P<0.0001), urinary sodium/potassium ratio (-0.62 vs. 0.06, P<0.0001), SBP (-1.2mmHg vs. 0.5mmHg, P=0.003) and DBP (-3.3mmHg vs. -2.4mmHg, P=0.04). At 36 months, there was a significant trend of greater SBP decrease with lower quintiles of achieved sodium excretion (P=0.005), but not with DBP (P=0.67). In analyses that corrected for measurement error, the estimated mean reduction in SBP from a 100mmol reduction in sodium was 7.0mmHg at 18 months and 3.6mmHg at 36 months. In other analyses limited to those with 24 hours at all time points, those individuals who maintained reduced sodium intake had significantly lower SBP compared to those who did not reduce their sodium intake. Study strengths include its design, high-quality control, and rigorous analytic methods. Limitations include attenuated adherence over time leading to a modest contrast between active and control groups. Overall, the observational analyses presented in this paper are consistent with dose-response trials, documenting that a dose-dependent relationship of SBP reduction with both the extent of sodium reduction and achieved levels of sodium.

Dickinson KM et al, 2009 (neutral quality). This randomized crossover study compared the effects of a low-salt (LS; 50mmol Na per day) diet with those of a usual-salt (US; 150mmol Na per day) diet on flow-mediated dilatation (FMD). Subjects included 29 overweight and obese normotensive Australian men and women who followed a LS diet and a US diet for two weeks. Participants received diet counseling on how to achieve the intended dietary goals. The diets were designed to ensure weight stability and had similar potassium and saturated fat contents. At the end of each two-week intervention, FMD, pulse wave velocity, augmentation index andBP were measured. The 24-hour sodium excretion was significantly lower (P=0.0001) with the LS diet (64.1±41.3mmol) than with the US diet (156.3±56.7mmol), while urinary potassium excretion was similar on both diets. Flow-mediated dilatation was significantly greater (P=0.001) with the LS diet (4.89%±2.42%) than with the US diet (3.37%±2.10%), SBP was significantly (P=0.02) lower with the LS diet (112±11 mmHg) than with the US diet (117±13mmHg). No significant changes in augmentation index or pulse wave velocity were observed. There was no correlation between change in FMD and change in 24-hour sodium excretion or change in BP. The authors concluded that salt reduction improved endothelium-dependant vasodilation in normotensive subjects independent from change BP; suggesting additional cardioprotective effects of salt reduction beyond BP reduction. Study limitations include the short duration of the intervention and relatively few BP measurements at the end of each feeding period. The effects of a reduced sodium intake on FMD suggest that higher sodium intake, in the range commonly consumed in the US, has deleterious effects on vascular function, apart from the well-known effects of increased sodium on BP.

Forrester T et al, 2005 (positive quality). This randomized crossover study examined the effect of low- and high-salt diets on BP response in 114 normotensive adults living in Nigeria (N=58) and Jamaica (N=56). After a four-week run-in period to determine willingness to adhere to a low-salt diet, subjects completed a two-period crossover study of low-salt (usual diet, 50mEq sodium) and high-salt intake (usual diet +50mEq sodium). Each period lasted three weeks, with a two-week washout that separated the periods. Participants were counseled to follow each diet. Baseline UNa excretion was 86.8 and 125.6mEq per day in Nigeria and Jamaica, respectively. Mean baseline SBP was 125mmHg in Jamaica and 114mmHg in Nigeria. Mean urinary potassium excretion was approximately 50mmol per day in both countries. After adjustment for baseline sodium excretion, period effects, age and sex, the net change in urinary sodium excretion between the low-salt and high-salt interventions was 72.2mEq per day in Nigeria and

78.8mEq per day in Jamaica. The mean difference between baseline sodium excretion and low-sodium phase was 33.6mEq per day in Nigeria and 57.5mEq per day in Jamaica. The mean change in SBP between the low- to high-sodium interventions in both countries was approximately 5mmHg suggesting that that the efficacy of sodium reduction in developing countries equals those noted in more affluent cultures. Study strengths include standardized BP measurements, rigorous methods and a cross-cultural comparison. Study limitations include the short duration of the intervention periods. Overall, this trial confirms that sodium reduction lowers BP in non-hypertensive individuals in two different countries with different levels of baseline sodium intake.

Gates PE et al, 2004 (neutral quality). This randomized, crossover study examined the effects of dietary sodium restriction on large elastic artery compliance and BP. Twelve untreated US adults (six men and six women; 64 + two years) with stage one systolic hypertension (HTN) were assigned to four weeks of low (57mmol per day) or normal (135mmol per day) sodium intake. Participants ate a reduced sodium diet in each period; the contrast in total dietary sodium intake was achieved with pills (either placebo or slow-release sodium chloride). The amount of pills was titrated to achieve the mean baseline levels of sodium intake. Urinary sodium excretion was reduced by 60% by the end of week one of sodium restriction (54±11mmol per day, P<0.01) vs. baseline (135±14). There was no consistent difference in carotid artery compliance between the low and usual sodium periods. During weeks two to four, 24-hour ambulatory SBP was reduced by approximately 6mmHg in the low compared to usual sodium period. Strengths of this study include multiple outcomes of potential interest, beyond BP. However, limitations were substantial and include a confusing presentation of data, mostly comparisons with baseline rather than comparisons between the low and usual sodium periods and suboptimal presentation of the achieved contrast in sodium. Overall, the results of this study should be viewed as non-contributory.

He FJ et al, 2009 (positive quality). This randomized, double-blind crossover trial, conducted in London, England, examined the effect of a modest reduction in salt intake on BP, 24-hour urinary albumin excretion and pulse wave velocity in three ethnic groups with untreated, mildly raised BP. Participants included 71 whites, 69 blacks and 29 Asians, aged 30 to 75 years, with sitting SBP of 140 to 170mmHg or DBP 90 to 105mmHg. All subjects consumed a reduced salt diet for the first two weeks of the study, then were randomized to either slow sodium or placebo for six weeks, followed by a crossover to the opposite tablets for an additional six weeks. From slow sodium to placebo, UNa was reduced by 55mmol per day, from 165+58 to 110+49mmol per 24 hours (9.7 to 6.5g per day salt, respectively). Blood pressure decreased from 146+13/91+8 to 141+12/88+9mmHg (P>0.001), urinary albumin from 10.2 (IQR: 6.8 to 18.9) to 9.1 (6.6 to 14.0) mg per 24 hours (P>0.001), albumin/creatinine ratio from 0.81 (0.47 to 1.43) to 0.66 (0.44 to 1.22) mg per mmol (P>0.001) and carotid-femoral pulse wave velocity from 11.5±2.3 to 11.1±1.9 m/s (P>0.01). Strengths of this trial include the diverse study population, the clear presentation of results and the duration of feeding. Limitations are the reporting of subgroup findings without interactions tests and suboptimal description of methods (e.g., source of participants, number of dropouts). Overall, this trial documents that sodium reduction, commonly tested in white and black populations, also lowers blood pressure in Asians with HTN and that the extent of BP appears similar in the subgroups tested (whites, blacks and Asians). Reductions in albuminuria and pulse wave velocity also suggest that sodium reduction has benefits beyond BP reduction.

He and MacGregor, Cochrane 2004, Updated in 2005 (positive quality) a systematic review and meta-analysis of 34 trials assessed the effect of modest salt reduction on BP and whether there is a dose response to salt reduction. Twenty-three trials were conducted with subjects who had elevated BP (N= 802) and 11 trials with normotensive subjects (N=2,220). MEDLINE, EMBASE, and Cochrane library databases were searched for randomized trials with a four-week duration or more (date range 1966 to June 2001; updated search through April 2005). Mean effect sizes were calculated using both fixed and random-effects models. The relationship between the change in UNa and the change in BP was examined using weighted linear regression. The net change in BP (Fixed Model) was -3.03mmHg for SBP and -1.76mmHg for DBP. In subjects with elevated BP, the median reduction in UNa was 78mmol per 24 hours (4.6g per day of salt), the mean reduction in BP was -5.06 for SBP and -2.70mmHg for DBP. In subjects with normal BP, the median reduction in urinary sodium was 74mmol per 24 hours (4.4g per day of salt) and the mean reduction in BP was -2.03mmHg for SBP and -0.99mmHg for DBP. Weighted linear regression showed a significant relationship between the reduction in urinary sodium and the reduction in BP. The dose response analysis with y-intercept fixed at zero showed a significant dose response to salt reduction for both SBP and DBP. A 100mmol reduction of sodium intake per day (6g salt) predicted a fall of 7.2mmHg for SBP and 3.8mmHg for DBP. This meta-analysis demonstrated that a modest reduction in salt intake for four weeks or more had a significant effect on BP in hypertensive and normotensive subjects. There was also a significant dose response relationship between sodium reduction and both systolic and diastolic blood pressure.

He J et al, 2009 (positive quality). This non-randomized, controlled three-week feeding trial, conducted in rural China, examined gender differences in BP response to dietary sodium and potassium intake. The interventions included seven days on a low-sodium diet (51.3 mmol per day), seven days on a high-sodium diet (307.8mmol per day) followed by seven days on a high-sodium (307.8mmol per day) plus potassium supplementation (60mmol per day), with no washout period between interventions. Subjects were 1,906 adults (1,010 men and 896 women), BP range 130 to 160mmHg SBP and 85 to 100mmHg DBP; including eligible siblings and offspring, aged 18 to 60 years, who participated in the Genetic Epidemiology Network of Salt Sensitivity (GenSalt) study. During the interventions, meals were cooked without salt. Staff added prepackaged salt to individual meals prior to serving and observed subjects' consumption. Food records were kept for each meal. Three-timed urine specimens were collected, one 24-hour and two overnight, at baseline and in each phase of the intervention to assess dietary compliance. Nine BP measurements were obtained during the three-day baseline observation and the last three days of each intervention using a random-zero sphygmomanometer. Compared to the low sodium arm, the high sodium arm raised SBP by 5.2mmHg in men and 6.3mmHg in women. The increase in SBP on the high compared to low sodium was less than zero in 73.9% of participants and more than four in

60.7%. Systolic BP responses to sodium increased with age, and both SBP and DBP responses to sodium and potassium interventions increased with baseline BP levels. Blood pressure responses to low and high sodium intervention were significantly greater (P<0.001) in women than in men. Study strengths include excellent compliance, inclusion of an arm with increased potassium, rigorous methods and conduct of a trial in an understudied, non-overweight population. Limitations include the short duration of each intervention phase (seven days), lack of a washout period, non-randomized order of diets, pre-post evaluation of the 'low sodium diet' and single ethnic group (rural Chinese). Overall, this study documents that increased salt intake raises BP in a generally lean Asian population.

Makela et al, 2008 (neutral quality). This RCT, conducted in Finland, assessed the effects of dietary sodium reduction on BP response and heart rate variability in 80 persons with essential hypertension (SBP of 160 to 200mmHg and DBP of 90 to 110mmHg). Forty persons were randomized to six months of a low-sodium diet (daily sodium intake reduced to less than 70mmol, general advice to lose weight if necessary, and general advice to reduce intake of saturated fats) and 40 were assigned to the control group (not described, but previously reported). Although BP was significantly reduced after six months in the sodium restriction group (SBP from 149.9±14.7 to 130.3±11.8mmHg, P<0.001 and DBP from 98.0±6.4 to 87.1±6.2mmHg, P<0.001), NS difference in the change between groups were detected. Additionally, no changes were seen in cardiac parasympathetic nervous control as measured by heart rate variability. Study strengths include the variety of measurements. Limitations include inadequate description of methods, approach to analysis with multiple BP over time, substantial differences between groups at baseline, and inconsistent description of BP results (e.g., significant time by group interaction in results, yet description of NS differences in BP change between groups). Overall, the results of this study should be viewed as non-contributory.

Pimenta et al, 2009 (positive quality). This randomized, crossover study, conducted in the US, examined the effects of dietary salt restriction on office and 24-hour ambulatory BP in 12 subjects with resistant HTN. Two one-week interventions, a low (50mmol per day) and high (250mmol per day) sodium diet, were separated by a two-week washout period. Potassium intake was high and similar in both diets (3,700mg in the 2,000kcal versions of the diets). Brain natriuretic peptide; plasma renin activity; 24-hour urinary sodium, potassium and aldosterone; 24-hour ambulatory BP monitoring; aortic pulse wave velocity; and augmentation index were compared. At baseline, subjects were on an average of 3.4 anti-hypertensive medications with a mean office BP of 145.8+10.8/83.9+11.2mmHg. Mean UNa excretion was 46.1+26.8mmol per day for the low-salt vs. 252.2+64.6 for the high-salt intervention. Office SBP and DBP decreased by 22.7 and 9.1mmHg, respectively, for the low- vs. high-salt diet. Plasma renin activity increased, whereas brain natriuretic peptide and creatinine clearance decreased during low-salt intake, indicative of intravascular volume reduction. Study strengths included the crossover, randomized design, use of 24-hour ambulatory BP monitoring and confirmation of dietary adherence with 24-hour urinary sodium excretion measurements. Limitations included the small number of subjects and short duration of the dietary treatment periods. Despite these limitations, this trial documents that sodium reduction lowers BP, even among individuals with resistant HTN who concurrently are taking multiple anti-hypertensive medications.

Schmidlin et al, 2007 (neutral quality). This non-randomized, cross-over trial conducted in the US tested the hypothesis that the sodium component of dietary sodium chloride can have a pressor effect apart from its capacity to complement the extracellular osmotic activity of chloride and plasma volume. The study lasted for 21 days total, with three consecutive seven-day periods: Two sodium-loading weeks separated by a sodium-restricted week. All participants (N=35 non-hypertensive blacks) consumed an eucaloric basal metabolic diet providing 30mmol of sodium and 45mmol of potassium per 70kg of body weight per day, as well as 20g water per kg of body weight per day during sodium restriction and 35g water per kg of body weight per day during sodium loading. Results were only presented in a stratified fashion (salt sensitive vs. salt resistant), not together. Study strengths include the research question, namely, the impact of the anion (chloride vs. bicarbonate) on BP. Limitations include the fixed order of diets and the focus on stratified results without presentation of overall results. Overall, the results of this study should be viewed as non-contributory.

Swift et al, 2005 (positive quality). This randomized crossover trial, conducted in the United Kingdom, determined the effects of moderate salt reduction on BP and urine protein excretion in 47 non-diabetic black hypertensive subjects. After a run-in period of four weeks of usual diet, followed by an additional run-in period of two weeks on a reduced salt (approximately 5g salt) diet, participants received either 12 slow-sodium tablets (10mmol sodium per tablet) daily to bring their salt intake back to normal or 12 placebo tablets daily for four weeks. In the 40 subjects who completed the study, reducing salt intake from approximately 10 to approximately 5g per day decreased BP from 159/101±13/8mmHg to 151/98±13/8mmHg (P<0.01). Mean protein excretion fell from 93 to 75mg per day (P<0.008). Study strengths include its crossover design and validity of measurements, while limitations include the narrow population, namely, black hypertensives. Overall, this trial documents that moderate salt reduction should lower proteinuria, as well as BP.

View table in new window

Author, Year, Study Design, Class, Rating	Subjects, Duration, and Location	Intervention Procedure	BP Measurement; Sodium Intake Measurement	Outcome (BP Values, mmHg)

Cappuccio F, Kerry S et al, 2006 Study Design: Cluster randomized trial Class: A Rating:	N=1,013 participants from 12 West African villages (628 women; 385 men). Mean age: 55 years. Average BP: 125/74mmHg. Average UNa: 101. Duration: Six months. Location: Africa.	Health promotion intervention was provided to examine the effect of education to reduce salt intake upon BP. All 12 villages received education on a wide range of public health topics. Sessions were conducted daily for the first week of the study and weekly thereafter. Intervention villages received additional advice to not add salt to food when cooking, to limit specific high-salt foods and to soak other high-salt foods in water overnight before eating. Height and weight were measured to determine BMI.	UNa excretion and BP levels were assessed at baseline, three and six months for all groups.	Relationship between salt intake (per 50mmol of UNa per day) and BP: • SBP: 2.17mmHg; 95% CI: 0.44 to 3.91; P<0.001 • DBP: 1.10mmHg; 0.08 to 1.94; P<0.001 • ΔSBP: -2.54mmHg; 95% Ci: -6.54 to 1.45 • ΔDBP: -3.95mmHg; 95% CI: -7.11 to -0.78; P=1.015. NS Δ in UNa excretion. However, in all participants, regardless of intervention, there was a consistent relationship between the ↓ in UNa excretion and the ↓ in BP when adjusting for confounders. A difference in 24-hour UNa of 50mmol was associated with a ↓ SBP of -2.12mmHg (-1.03 to -3.21) at three months and -1.34mmHg (-0.08 to -2.60) at six months (both P<0.001).
China Salt Substitute Study Collaborative Group 2007 Study Design: Randomized Controlled Trial Class: A Rating:	N=608 high-risk individuals; 585 subjects completed the trial, 292 in the salt-substitute group and 293 in the salt group. Duration: One year. Location: Rural northern China.	Trial examined replacement of salt used in home cooking with salt substitute and the effect on BP. Subjects randomized to salt or salt substitute for all home cooking x 12 months. Reduced-sodium, high-potassium salt substitute (65% NaCl, 25% KCl, 10% magnesium sulfate). Normal salt (100% NaCl).	First morning UNa and K at baseline, six and 12 months. BP measured with Omron automatic sphygmomanometer at baseline, one, two, three, six, nine and 12 months. Dietary salt or substitute used in cooking was assessed by self-report in terms of remaining proportion of home cooking salt from the start of the study remaining.	Mean difference in SBP between groups was 3.7mmHg (95% CI: 1.6 to 5.9, P<0.001). SBP was significantly ↓ in the salt substitute group than in the normal salt group at the six, nine and and 12-month visits (all P<0.02). The magnitude of this reduction ↑ over time (P=0.001) with the maximum net reduction of -5.4mmHg (-2.3 to -8.5) achieved at 12 months. There were no detectable effects on DBP at any time point or overall, and no evidence of any evolution of a difference over time.

Cook NR, Kumanyika SK et al, 2005 Study Design: Randomized controlled trial Class: A Rating:	1,157 overweight, non-hypertensive men and women were randomized and 880 subjects completed the three-year trial (437 in the sodium reduction interventions; 443 in usual care). Duration: Three years. Location: US.	Trials of Hypertension Prevention (TOHP) Phase II sodium intervention. The original TOHP II subjects were assigned to receive one of the following: • Counseling for weight loss only • Counseling for Na intake reduction to 80mmol per day • Counseling for weight loss and Na intake reduction to 80mmol per day • Usual care (UC) with no study-delivered intervention. Sodium intervention and UC groups were combined for analysis.	Na and K intake during trials estimated from a mean of three to seven 24-hour urinary excretions. Dietary Na intake also estimated from self-reported intake on follow-up questionnaire.	At 36 months, there were significant differences between the Na reduction group and UC group in Δ of UNa excretion (-50.9mmol vs. -13.2mmol per day, P<0.0001), urinary Na/K ratio (-0.62 vs. 0.06, P<0.0001), SBP (-1.2mmHg vs. 0.5mmHg, P=0.003), and DBP (-3.3mmHg vs. -2.4mmHg, P=0.04). At 36 months, there was a significant trend of greater SBP ↓ with lower quintiles of Na excretion (P=0.005), but not with DBP (P=0.67).
Dickinson K, Keough J et al, 2009 Study Design: Randomized crossover trial Class: A Rating:	N=29 adults (seven men, 22 women). Age: 52.7±6.0 years. Overweight or obese; BMI range 42.0 to 64.0kg/m^2. Normotensive. Duration: One month. Location: Australia.	Compared the effects of low-salt (LS; 50mmol Na per day) diet with usual-salt (US; 150mmol Na per day) diet on flow-mediated dilataion (FMD). Diets designed for weight stability and similar K and saturated fat contents. 24-hour urine to measure Na and K at baseline and end of each intervention.	ANOVA repeated measures used with and without covariates, including diet order, BP and baseline Na excretion. Pearson correlation used to assess association of Δ between variables. Brachial artery flow mediated dilatation measured after an overnight fast with a 7.5-MHz linear array transducer. Pulse wave velocity by Doppler measures at the carotid and femoral arteries. Augmentation index measured with SphygmoCor BP system. BP measured with automated	FMD: • US diet (3.37±2.10%) • LS diet (4.89±2.42%) significantly ↑ (P=0.001). SBP: • US diet (117±13mmHg) • LS diet (112±11mmHg), significantly ↓ (P=0.02). 24-hour UNa: • US diet (156.3±56.7mmol) • LS diet (64.1±41.3 significantly ↓ (P=0.0001). Pulse wave velocity (m/s): • US diet: 10.49 (3.07) • LS diet: 10.49 (4.14), No Δ (P>0.05).

			sphygmomanometer.	
Forrester T, Adeyemo A et al, 2005 Study Design: Randomized crossover trial Class: A Rating:	N=114 adults from Nigeria (N=58; 34 men, 24 women) and Jamaica (N=56; 34 men, 22 women). Age: 25 to 55 years, (Mean age: Nigeria, 46.6 years; Jamaica, 40.8 years). BMI: Nigeria, 23.1kg/m^2; Jamaica 28.5kg/m^2. Baseline BP normotensive: SBP Nigeria = 125mmHg; SBP Jamaica = 114mmHg. Baseline UNa excretion: Nigeria = 86.8mEq per day; Jamaica = 125.6mEq per day. Duration: Three months Location: Jamaica and Nigeria.	High salt diet: 50mEq ↑ in Na over usual diet at baseline. Low salt diet: 50mEq ↓ in Na from usual diet at baseline. Compared effects of low and high salt diet on mean BP response. After a two-week low-Na diet to assess ability for compliance, subjects had a one- to two-week period with usual diet. Subjects were then randomized to either a high- or low-salt diet for three weeks with a two-week usual diet wash out between crossover to the other three-week study arm.	24-hour urine obtained at baseline and end of each intervention; assayed for Na and K to assess dietary compliance. The following parameters were measured at each clinic visit. BP using both manual manometer and the Omron automatic device. Weight to nearest 0.1kg. Height, waist and hip circumference to nearest 0.1cm.	Net Δ in UNa excretion between the low-salt and high-salt interventions (adjusted for baseline UNa excretion, period effects, age and sex). • Nigeria: 72.2mEq per day • Jamaica: 78.8mEq per day. There were no net Δs in urinary K. Mean Δ in BP mmHg; average of manual and Omron measures (95% CI). ΔSBP • Nigeria: 4.5 (1.6, 7.3) • Jamaica: 5.5(3.0, 8.0). ΔDBP • Nigeria: 2.7 (0.9, 4.5) • Jamaica: 2.8 (0.5, 5.0).
Gates P, Tanaka H et al, 2004 Study Design: Randomized controlled trial Class: A Rating:	N=12 untreated older adults (six men, six women) with stage one systolic HTN. Age: 64±2 years. Duration: Eight weeks. Location: US.	Subjects were randomized to four-week periods of reduced and normal Na intake. All subjects consumed ↓ Na diets and took a prescribed number of tablets with each meal, either placebo or slow-release NaCl. The number of tablets taken was based on a once-weekly 24-hour UNa excretion compared to the average of two baseline samples. Subjects received comprehensive dietary education and counseling (at baseline and weekly) to reduce Na intake without Δ in caloric intake or dietary	Carotid artery compliance and β-stiffness index were determined using high-resolution B-mode ultrasound and simultaneous estimates of carotid BP using applanation tonometry. Casual brachial artery BP measurements were made after an overnight fast in the upright seated and supine positions. Ambulatory BP measurements were made during normal daily activity. Dietary assessment was based on three-day diet records with Food Processor	UNa excretion: • Baseline: 135±14mmol per day • Week one of Na restriction: 54±11mmol per day, P<0.01; a ↓ of 60%. Carotid artery compliance: • Baseline: 0.11±0.01mm per mmHg • Low-Na Week One: 0.14±0.02, P<0.05) an ↑ of 27% • Low-Na Week Two: +46%, to 0.16±0.02, P<0.01. Supine resting brachial artery SBP was ↓ by >5mmHg by week one of Na restriction, attaining peak reductions by week two (-12mmHg, P<0.01 vs. baseline). The 24-hour ambulatory SBP was ~3mmHg lower at week one of Na restriction

		composition.	software (ESHA) at baseline and the end of each intervention.	and ~6mmHg lower by week two (P<0.01 vs. baseline).
He Feng J, Marciniak M et al, 2009 Study Design: Randomized, double-blind, crossover trial Class: A Rating:	N=169 subjects, from three ethnic groups: • 71 whites • 69 blacks • 29 Asians. Age: 30 to 75 years. With untreated, mildly raised BP: Sitting SBP 140 to 170 or DBP 90 to 105mmHg. Duration: 14 weeks. Location: England.	All subjects consumed a reduced salt diet for the first two weeks. Then they were randomized to slow Na (90mmol per day plus low-Na diet) or placebo for six weeks, followed by a crossover to the opposite tablets for an additional six weeks. Measures were taken at end of each six-week intervention.	BP: 24-hour BP measured with Spacelabs 90207 devices. Mean of two consecutive 24-hour urines measured for urinary Na, K, creatinine, calcium and albumin excretion. Urinary albumin measured by laser immunonephelometry. Samples with measured concentrations less than 2.1mg per L werere-analyzed using a high-sensitivity ELISA. Carotid-femoral pulse wave velocity was measured non-invasively using an automatic device; outcome was mean of 10 cardiac cycles.	From slow Na to placebo, UNa was ↓ by 55mmol per day, from 165±58 to 110±49mmol per 24 hours (9.7 to 6.5g per day salt, respectively). BP ↓ from 146±13/91±8 to 141±+2/88±9 mmHg (P>0.001). Urinary albumin from 10.2 (IQR: 6.8 to 18.9) to 9.1 (6.6 to 14.0) mg per 24 hours (P>0.001). Albumin/creatinine ratio from 0.81 (0.47 to 1.43) to 0.66 (0.44 to 1.22) mg per mmol (P>0.001). Carotid-femoral pulse wave velocity from 11.5±2.3 to 11.1±1.9 m/s (P>0.01). Subgroup analysis found significant ↓ in BP and urinary albumin/creatinine ratio in all groups. The ↓ in pulse wave velocity was significant only in the black ethnic group.
He J, Gu D et al, 2009 Study Design: Non-randomized trial Class: M Rating:	N=1,906 adults, eligible offspring and siblings (men 1,010; women 896). Mean BP (mmHg): Men = 115±12.8/75±9.9; Women = 114.9±15.4/71±71.7. Duration: 24 days. Location: China.	Trial examined gender differences in the association between dietary Na and K intake and BP. Three 7-day dietary interventions: • Low Na (51.3mmol per day) • High Na (307.8mmol per d) • High Na (307.8mmol per day) plus 60mmol K supplement. All meals were provided and consumption was	BP measured at three-day baseline, last three days of each intervention using a random-zero SM. Na intake estimated from food records; 24-hour urinary excretions of Na and K at baseline and each of the three intervention phases.	Δs in BP response were significantly greater in women than in men (all P<0.001). *Low-sodium diet* ΔSBP: • Women: -8.1mmHg (95% CI: -8.6 to -7.6) • Men: -7.0 (-7.5 to -6.6) ΔDBP: • Women: 4.5 (-4.9 to -4.1) • Men: -3.4 (-3.8 to -3.0). *High-sodium diet* ΔSBP: • Women: 6.4 (5.9 to 6.8) • Men: 5.2 (4.8 to 5.7).

		supervised.		ΔDBP: • Women: 3.1 (2.7 to 3.5) • Men: 1.7 (1.4 to 2.1).
Makela P, Vahlberg T et al, 2008 Study Design: Randomized controlled trial Class: A Rating:	N=80 subjects with mild to moderate essential HTN on non-pharmacological Na restriction. Forty subjects randomized to a low Na diet; 40 assigned to the control group. Duration: Six months. Location: Finland.	Subjects were randomized to a low-Na diet (↓ of daily Na intake to less than 70mmol, general advice to lose weight, if necessary and general advice to ↓ intake of saturated fats) or control group (intervention not described).	BP measured at one-month intervals throughout the study. Na intake was estimated three times during the study, at zero, three and six months. Intake was estimated from seven-day food records using Nutrica software from the Social Insurance Institution, Finland. 24-hour UNa and K excretion was also collected and measured by flame photometry. 24-hour ambulatory ECG carried out at beginning of study and at six months; analyzed with Oxford Medilog Series 4.24. Heart rate variability (HRV): Five time-domain variables were analyzed.	BP ↓ significantly more in intervention group. SBP: 149.9±14.7 to 130.3±11.8mmHg. DBP: 98.0±6.4 to 87.1±6.2mmHg, P<0.001. However, NS differences in the Δ between groups could be detected. 24-hour UNa ↓ significantly (P<0.001) in intervention group, but ↑ in the control group (time x group, P<0.001). NS Δs or differences in Δs were seen in any time or frequency-domain variables of heart rate variability. No correlation in Δs of HRV was found in relation to Na intake during the study.
Pimenta E, Gaddam KK et al, 2009 Study Design: Randomized, crossover trial Class: A Rating:	N=12 subjects with resistant HTN. • Eight females • Four males. • Six blacks • Six whites. Age: 55.5±9.4 years. On average, 3.4 antihypertensive medications. Duration: One month. Location: US.	Examined the effects of dietary salt restriction on office and 24-hour ambulatory BP. Two one-week dietary Na interventions separated by a two-week washout period: • Low (50mmol per day) • High (250mmol per day).	Office and 24-hour ambulatory BP monitoring with ABPM monitor (Suntech). 24-hour urine collected to measure urinary Na and K excretion, as well as aldosterone and creatinine. Morning blood specimens analyzed for serum potassium, brain natriuretic peptide, plasma aldosterone, plasma renin activity and urinary aldosterone	Mean UNa excretion: • Low Na: 46.1±26.8mmol per day • High Na: 252.2±64.6mmol per day. ΔBP for the low- vs. high-salt intervention: • ΔSBP: -22.7mmHg • ΔDBP: - 9.1mmHg. Plasma rennin activity ↑, whereas brain natriuretic peptide and creatinine clearance ↓ during low-salt intake.

			measured by radioimmunoassay. Aortic pulse wave velocity and augmentation index measured with SphygmoCor system.	
Schmidlin O, Forman A et al, 2007 Study Design: Non-Randomized Controlled Trial Class: C Rating: 	N=35 black adults. Salt Sensitive (SS): N=18 (51%; 17 males and one female). Salt Resistant (SR): N=17 (49%; 15 males and two females). After adjusting for age and BMI, the SS subjects' DBP and MAP were significantly different than the SR subjects (P≤0.05). Duration: 21 days Location: US.	Two 7-day Na-loading interventions separated by a Na restricted week. Interventions included: • NaCl supplement: 250mmol per 70kg weight per day (≤300mmol per day) • $NaHCO_3$ supplement: 250mmol per 70kg weight per day (≤300mmol per day) • Placebo tablets. All participants consumed a eucaloric basal metabolic diet providing 30mmol of Na and 45mmol of K per 70kg of body weight per day. Subjects consumed 20g water per kg body weight per day during Na restriction and 35g per kg per day during Na loading.	Daily BP measured every four-hours with automated oscillometric device (Dinamap, Criticon Inc.); average calculated. MAP = average of Na restriction days five and six, subtracted from average of days five and six during Na loading with either NaCl or Na HCO_3. Daily 24-hour urine analyzed for Na, Cl and Creatinine. Cumulative Na excretion (week three only): Corrected for creatinine excretion; adjusted for 70kg weight. SS defined as an NaCl-induced ↑ in MAP of at least 5mmHg. Weight measured daily at 6 a.m. Blood samples (by stand-on on last day of each intervention): Plasma renin activity, aldosterone, creatinine hematocrit and serum electrolytes.	In SS (but not SR), BP varied directly and highly significantly with the serum concentration of Na. Average NaCl-induced MAP: SS, 11±2mmHg; SR, 1±2mmHg. MAP ↑ significantly from 90mmHg on low NaCl to 95mmHg with $NaHCO_3$ and to 101mmHg with NaCl. The pressor effect of NaCl strongly predicted that of $NaHCO_3$. In SS subjects, MAP varied directly with plasma Na concentration attained with all Na loading. Both NaCl and $NaHCO_3$ induced similar significant ↑ in body weight in SS and SR. Both NaCl and $NaHCO_3$ induced significant ↓ in hematocrit values in SS and SR, but were significantly larger with NaCl than $NaHCO_3$. NaCl-induced ↓ in PRA (but not aldosterone) was slightly, but significantly greater in SR than in SS.
Swift PA, Markandu ND et al, 2005 Study Design: Randomized crossover trial	N=40 non-diabetic black subjects. Hypertensive: SBP≥40mmHg; DBP≥90mmHg. Age: 50±10 years.	Initial run-in periods on usual (four weeks) and reduced salt (~5g salt) diets (two weeks). Then subjects received either 12 slow-Na tablets (10mmol Na per	BP and other measurements were made at the end of each run-in period and intervention by trained nursing staff. 24-hour ambulatory	Reducing salt intake from ~10g to ~5g per day ↓ BP: SBP 8±13mmHg, P<0.001; DBP 3±7mmHg, P<0.009. Mean ↓ in urinary protein

Class: A Rating:	BMI: 28±4kg/m2. Duration: 3.5 months. Location: United Kingdom	tablet) daily to bring their salt intake back to normal or 12 placebo tablets daily for four weeks, then crossed over.	BP was performed using SpaceLab 90207 devices, which were fitted in the mornings. BP recordings taken at half-hour intervals from 9 a.m. to 10 p.m. and at hourly intervals from 10 p.m. to 9 a.m.	excretion with salt reduction: 18±39mg per 24 hours (P<0.008). Relationship between urinary protein excretion and BP: • SBP (R=0.07; P=0.70) • DBP (R=0.19; P=0.26). **Other Findings** Significant ↓ in mean daytime and nighttime ABPs, with the ↓ in salt intake (mean 24-hour ↓ of 7/3mmHg).

Research Design and Implementation Rating Summary
For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

Cappuccio FP, Kerry SM, Micah FB, Plange-Rhule J, Eastwood JB. A community programme to reduce salt intake and blood pressure in Ghana [ISRCTN88789643]. A community programme to reduce salt intake and blood pressure in Ghana [ISRCTN88789643]. *BMC Public Health.* 2006 Jan 24; 6: 13. PMID: 16433927.

China Salt Substitute Study Collaborative Group. Salt substitution: A low-cost strategy for blood pressure control among rural Chinese. A randomized, controlled trial.*J Hypertens.* 2007 Oct; 25 (10): 2,011-2,018.

Cook NR, Kumanyika SK, Cutler JA, Whelton PK; Trials of Hypertension Prevention Collaborative Research Group. Dose-response of sodium excretion and blood pressure change among overweight, nonhypertensive adults in a three-year dietary intervention study. *J Hum Hypertens.* 2005 Jan; 19(1): 47-54.

Dickinson KM, Keogh JB, Clifton PM. Effects of a low-salt diet on flow-mediated dilatation in humans. *Am J Clin Nutr.* 2009 Feb; 89 (2): 485-490.

Forrester T, Adeyemo A, Soarres-Wynter S, Sargent L, Bennett F, Wilks R, Luke A, Prewitt E, Kramer H, Cooper RS. A randomized trial on sodium reduction in two developing countries. *J Hum Hypertens.* 2005 Jan; 19(1): 55-60.

Gates PE, Tanaka H, Hiatt WR, Seals DR. Dietary sodium restriction rapidly improves large elastic artery compliance in older adults with systolic hypertension. *Hypertension.* 2004 Jul; 44 (1): 35-41.

He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. *Cochrane Database Syst Rev.* 2004; (1): CD004937. PMID: 15266549

He Feng J, Marciniak M, Visagie E, Markandu ND, Anand V, Dalton RN, MacGregor GA. Effect of Modest Salt Reduction on Blood Pressure, Urinary Albumin and Pulse Wave Velocity in White, Black and Asian Mild Hypertensives.*Hypertension* Sep 2009.

He J, Gu D, Chen J, Jaquish CE, Rao DC, Hixson JE, Chen JC, Duan X, Huang JF, Chen CS, Kelly TN, Bazzano LA, Whelton PK; GenSalt Collaborative Research Group. Gender difference in blood pressure responses to dietary sodium intervention in the GenSalt study.*J Hypertens.* 2009 Jan; 27(1): 48-54.

Makela P, Vahlberg T, Kantola I, Vesalainen R, Jula A. The effects of a six-month sodium restriction on cardiac autonomic function in patients with mild to moderate essential hypertension.*Am J Hypertension.* 2008; 21: 1,183-1,187.

Pimenta E, Gaddam KK, Oparil S, Aban I, Husain,Dell'Italia LJ, Calhoun DA. Effects of Dietary Sodium Reduction on Blood Pressure in Subjects With Resistant Hypertension Results From a Randomized Trial. *Hypertension.* 2009 Jul 20. [Epub ahead of print]

Schmidlin O, Forman A, Sebastian A, Morris RC Jr. Sodium-selective salt sensitivity: its occurrence in blacks. *Hypertension.* 2007 Dec; 50 (6): 1,085-1,092. Epub. 2007 Oct. 15.

Swift PA, Markandu ND, Sagnella GA, He FJ, MacGregor GA. Modest salt reduction reduces blood pressure and urine protein excretion in black hypertensives: A randomized control trial. *Hypertension*. 2005 Aug; 46(2): 308-312. Epub 2005